UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/811,292	03/26/2004	Brett Allison	PRD2053	2156

27777 7590 07/27/2006

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
SOLOLA, TAOFIQ A	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 07/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/811,292	ALLISON ET AL.	
	Examiner	Art Unit	
	Taofiq A. Solola	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 1-32 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 1-32 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 1.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-32 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

"'In the context of determining whether sufficient "utility as a drug, medicant, and the like in human therapy" has been alleged, It is proper for the examiner to ask for substantiating evidence unless one with ordinary skill in the art would accept the [process of making and the utilities] as obviously correct." *In re Jolles*, 628 F.2d 1327; 1332 (Fed. Cir. 1980), citing *In re Novak*, 306 F.2d 924 (CCPA 1962); see Application of Irons, 340 F.2d 974, 977-78 (CCPA 1965). "A specification disclosure which contains a teaching of the manner and process of making and using the invention . . . must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995), Id. at 1566, quoting *Marzocchi*, 439 F.2d 220, 223 (CCPA 1971); *Fiers v. Revel,* 984 F.2d 1164, 1171-72 (Fed. Cir. 1993), quoting *Marzocchi*, 439 F.2d at 223; see also *Armbruster*, 512 F.2d 676, 677 (CCPA 1975); *Knowlton*, 500 F.2d 566, 571 (CCPA

1974); *Bowen*, 492 F.2d 859 (CCPA 1974); *Hawkins*, 486 F.2d 569, 576 (CCPA 1973). Where there is "no indication that one skilled in the art would accept without question [the instant process of making and method of use] and no evidence has been presented to demonstrate that the claimed products do have those effects *Novak*, 306 F.2d at 928, an applicant has failed to sufficiently demonstrate sufficient utility and therefore cannot establish enablement."' *In re Rasmusson,* 75 USPQ2d 1297 (CAFC 2005). The claimed utilities are not believable for the following reasons:

For rejection under 35 U.S.C. 112, first paragraph, the following factors must be considered. *In re Wands*, 8 USPQ2d 1400, 1404 (CAFC, 1988): 1) Breadth of claims, 2) Nature of invention, 3) State of prior art, 4) Level of ordinary skill in the art, 5) Level predictability in the art, 6) Amount of direction and guidance provided by the inventor, 7) Existence of working examples, 8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breath of the claimed invention involves method of using instant compounds. The nature of the invention is in the field of medicine wherein applicant claims method of using compounds to treat or prevent CCK2 mediated diseases. According to Tullio et al., *Expert Opinion on Investigational Drugs,*(2000), Vol. 9(1), pages 129-146, "the therapeutic applications of CCK-BR [CCK2] antagonists remain , at present , unclear. . . Further studies are needed to define whether CCK-BR antagonists could be useful in the treatment of CNS diseases . . ." On CCK-BR agonists, the group states "much information remains to be discovered." Tullio et al., conclude: "the role of CCK in many different physiological processes has led to interest regarding biological as well as possible therapeutic role of CCK receptor ligands. Despite many different studies, the literature concerning the behavioral actions of CCK and CCK receptor ligands appears sometimes broad, with much inconsistency and discrepancy." See page 141,

column 2. According to Rosario Herranz in *Medicinal Research Reviews*, (2003), Vol. 23(5), page 559-605,

> domains adjacent to the extracellular space.[29,56–58] In spite of the high level of homology in the amino acid sequence for each CCK receptor subtype among species (72–80%), minor species-specific differences in receptor structure and distribution do occur that can result in significant pharmacological and physiological differences. In fact, mutagenesis studies in CCK receptors have shown that single amino acid substitutions may change ligand affinity[59,60] and, even, the agonist/antagonist functionality,[61] which in turn explain species-related differences. Therefore, it is important to consider the appropriate species for the intended experimental goals, and to be careful before extrapolating data from one animal species to another. Recently, several single nucleotide poly-

> Over the past 15 years, the search of CCK receptor ligands has evolved from the initial CCK structure derived peptides towards peptidomimetic or non-peptide agonists and antagonists with improved pharmacokinetic profile. This research has provided a broad assortment of potent and highly selective antagonists for both CCK receptor subtypes, CCK_1 and CCK_2, of diverse chemical structure. These antagonists, as pharmacological tools, have highly contributed to the characterization and localization of CCK receptor subtypes, as well as to the study of physiological and pathological actions of CCK. However, despite the progress in this field, the complex biological effects of CCK mediated by CCK_1 and CCK_2 receptors are not yet completely established. Particularly, additional research is necessary for gaining insight into the complex system of interaction of CCK with other neurotransmitters both in the CNS and in the periphery. Pharmacological research is also necessary to confirm that the different binding affinities determined for some antagonists by using different radioligands, and in some cases the discrepancies observed between binding potency and antagonistic potency, are due to the existence of different binding states and not to receptor subtype heterogeneity.

See page page 563, lines 1-8 and page 591, the conclusions. The state of the prior art is what prior art knows about the nature of the invention. It is well documented that CCK1 and CCK2 receptors are widely distributed in the tissues such that inhibition or activation of a receptor often have unexpected effects due to inhibition and/or activation of unrelated receptor sites. See Tullio et al., *ibid,* page 129, the introduction and Rosario Herranz, *ibid,* the abstract. No prior art teaches prevention of the claimed utilities. Also, most of the specific diseases in claims 31-32 are not preventable. The level of ordinary skill in the art is such that the enumerated problems above are not yet resolved. The predictability or lack thereof in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. The lower the predictability, the higher the direction and guidance that must

be provided by applicant. In the instant invention the predictability is very low and consequently, the need for higher levels of direction and guidance by applicant. However, there is no evidence in the specification that applicant has resolved above CCK-associated problems, particularly CCK2. There is no evidence in the specification that established correlation between pK_1 or guinea pig gastric corpeal muscle contraction disclosed in the specification, and the instantly claimed utilities. *See Ex parte Mass*, 9 USPQ2d 1746, 1987. The specification fails to set forth how a "normal" person predisposed to the diseases is identified, screened and treated so as to prevent occurrence of any of the diseases in the first place.

In addition, inhibition and/or activation of CCK-2 receptor could be due to damage and/or mutation at the receptor site. See Rosario Herranz, *ibid,* reproduced statement above. To use the instant invention as claimed, one of ordinary skill in the art would have to perform significant amount of experimentation to resolve the enumerated problems above, must determine if inhibition and/or activation of CCK-2 receptor is due to damage and/or mutation at the receptor site. These assays must be performed in every instant of using the compounds. Therefore, the quantity of experimentation required to use the compound as claimed, based on applicant's limited disclosure would be undue burden because, one of ordinary skill in the art would have to perform significant amount of experiments.

MPEP 2164.01(a) states, "[a] conclusion of lack of enablement means that, based on the evidence regarding any of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. The purpose of 35 USC 112 is to obviate the need for this type of experimentation. *In re Borkowski,* 164 USPQ

642 (CCPA,1970). See also, *Univ. of Rochester v. G.D.Searle & Co,* 68 USPQ2d 1424 (DC WNY, 2003). By deleting the claims the rejection would be overcome.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Several phraseologies in claims 1-2, 13, 29-32 are confusing and therefore, the claims are indefinite. For example, the following phraseologies in claim 1 are confusing:

b) naphthyl-(CR^s_2)-, benzoylC_{0-3}alkyl-(CR^s_2)-, phenyl, said phenyl optionally fused at two adjacent carbon atoms to R^f, phenyl-(CR^s_2)-, said phenyl optionally fused at two adjacent carbon atoms to R^f,

f) Ar^{6-5}-(CR^s_2)-, where Ar^{6-5} is phenyl having the point of attachment and fused to a 5-membered heteroaryl having 1 heteroatom member selected from the group consisting of O, S, >NH or $>NC_{1-4}$alkyl and having 0 or 1 additional heteroatom member which is -N=,

iv) a 4-7 membered heterocyclic ring said heterocyclic ring having 0 or 1 additional heteroatom members separated from the nitrogen of attachment by at least one carbon member and selected from O, S, -N=, >NH or >NR^p, having 0, 1 or 2 unsaturated bonds, having 0, 1 or 2 carbon members which is a carbonyl and optionally having one carbon member which forms a bridge, the heterocyclic ring fused at two adjacent carbon atoms forming a saturated bond or an adjacent carbon and nitrogen atom forming a saturated bond to a 4-7 membered hydrocarbon ring, having 0 or 1 possibly additional heteroatom member, not at the ring junction, selected from O, S, -N=, >NH or >NR^p, having 0, 1 or 2 unsaturated bonds, having 0, 1 or 2 carbon members which is a carbonyl and having 0, 1 or 2 substituents R^p;

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Weinstock et al., WO/2000078145.

Weinstock et al., disclose the marked compound in the attached abstract.

Claims 1-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Petrov et al., Meditsinskaya Parazitologiya I Parazitarnye Bolexni, (1996) Vol. 4, pages 40-42.

Petrov et al., disclose the marked compounds in the attached abstract.

Claims 1-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Mikhailitsyn et al., Meditsinskaya Parazitologiya I Parazitarnye Bolexni, (1991) Vol. 6, pages 52-53.

Mikhailitsyn et al., disclose the marked compounds in the attached abstract.

Claims 1-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Mikhailitsyn et al., Meditsinskaya Parazitologiya I Parazitarnye Bolexni, (1991) Vol. 2, pages 36-38.

Mikhailitsyn et al., disclose the marked compounds in the attached abstract.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over all the prior arts cited above, individually.

Applicant claims composition of the compounds of formula I.

Determination of the scope and content of the prior art (MPEP ∋2141.01

Each prior art teach a method of using the marked compounds in the attached abstract.

Ascertainment of the difference between the prior art and the claims (MPEP ∋2141.02)

The difference between the instant invention and that of the prior arts is that applicant claims a composition while the prior arts each teach a method of using the composition.

Finding of prima facie obviousness--rational and motivation (MPEP ∋2142.2413)

However, to practice the methods of using the compounds, the compounds must necessarily be in form of a composition. Therefore, the instant invention is prima facie obvious from the teachings of the prior arts. One of ordinary skill in the art would have known to claim the composition instead of the method of using the composition at the time the invention was made. The motivation is from knowing that the compound is used as a composition.

Objection

Tables must be removed in claims 27-28 and the compounds rewritten in accordance with the US patent practice.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taofiq A. Solola, PhD. JD., whose telephone number is (571) 272-0709.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph McKane, can be reached on (571) 272-0699. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

TAOFIQ SOLOLA
PRIMARY EXAMINER
Group 1626

July 19, 2006